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3-17-04

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| Appellants: | Thomas Jozefiak, Stephen Randall Holmes-Farley, W. Harry Mandeville, III, Chad Cori Huval, Venkata R. Garigapati, Keith K. Shackett and Danny Concagh | | |
| Application No.: | 09/721,291 | Group: | 1617 |
| Filed: | November 22, 2000 | Examiner: | Wang, Shengjun |
| Confirmation No.: | 5051 | | |
| For: | FAT-BINDING POLYMERS | | |

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BRIEF ON APPEAL

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This Brief on Appeal is submitted pursuant to the Notice of Appeal received in the U.S. Patent and Trademark Office on July 31, 2003, and in support of the appeal from the final rejection of Claim 71 and 73 set forth in the Office Action mailed on February 26, 2003. The fee for filing a brief in support of an appeal is enclosed. A Petition for Extension of Time and the appropriate fee are being filed concurrently. The balance of the Appeal Brief is set forth under the appropriate headings, as specified by 37 C.F.R. § 1.192(c).

I. REAL PARTY IN INTEREST

The real party in interest is Genzyme Corporation, 1 Kendall Square, Cambridge, Massachusetts 02149. Genzyme Corporation is the Assignee of the entire right, title and interest in the subject application, by virtue of an Assignment recorded on October 16, 1999 at Reel

010300, Frames 0475-0480 (from Appellants to GelTex Pharmaceuticals, Inc.) and an Assignment recorded on May 5, 2003 at Reel 014022, Frames 0197-0207 (from GelTex Pharmaceuticals, Inc. to Genzyme Corporation).

II. RELATED APPEALS AND INTERFERENCES

Appellants, the undersigned Agent and Assignee are not aware of any related appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF CLAIMS

Claims 1-41, 49-55, 62-70, 72 and 74-76 are canceled.

Claims 42-48, 56-61, 71 and 73 are pending.

Claims 42-48 and 56-61 are allowed.

Claims 71 and 73 have been finally rejected and are subject to appeal. Claims 71 and 73 were amended in the Amendment filed on November 19, 2002.

Claims 49-55 and 76 were mistakenly canceled in the Amendment filed November 19, 2002 and were resubmitted as Claims 77-84 in the Amendment After Final filed June 26, 2003. However, the Amendment After Final was not entered by the Examiner.

A copy of the claims involved in the Appeal is present in the Appendix to this Brief.

IV. STATUS OF AMENDMENTS

An Amendment After Final was mailed on June 26, 2003. No claims were amended, although new Claims 77-84 were added (corresponding to original Claims 49-55 and 76). The amendments were not entered by the Advisory Action dated July 18, 2003 (Paper No. 14).

V. SUMMARY OF INVENTION

The claimed invention relates to a method of treating obesity, a method for reducing the absorption of dietary fat, and a method for treating hypertriglyceridemia in a mammal comprising administering to a mammal polymers characterized by a repeat unit represented by Structural Formula (VI) or Structural Formula (VII), as well as pharmaceutical compositions comprising

these polymers (page 2, lines 18-21, page 20 and page 23, line 28 through page 24, line 6 of the Specification).

The allowed claims are directed to a method of treating obesity, a method for reducing the absorption of dietary fat, and a method for treating hypertriglyceridemia in a mammal comprising administering to the mammal a polymer characterized by a repeat unit represented by Structural Formula (VI) or Structural Formula (VII).

The finally rejected claims, Claims 71 and 73, which are subject to appeal are directed to pharmaceutical compositions comprising an inert pharmaceutical adjuvant material and a polymer characterized by a repeat unit represented by Structural Formula (VI) or Structural Formula (VII).

VI. ISSUES

The sole issue on appeal, as understood by Appellants, is:

(1) Whether Claims 71 and 73 are properly rejected under 35 U.S.C. § 103(a) as being obvious over JP 04-333694 (Niike, *et al.*).

VII. GROUPING OF CLAIMS

With respect to the issue on appeal, the pending claims do not stand or fall together. Pending Claims 71 and 73 should be grouped separately for purposes of the appeal, as the claims are separately patentable:

Group 1 - Claim 1

Group 2 - Claim 2.

VIII. ARGUMENT

A. Summary of the Examiner's Rejection

The Examiner stated in the Office Action mailed February 26, 2003 that Niike, *et al.* teach a copolymer of methacrylate ester and an ammonium bearing monomer, where the monomer is a substituted diallylammonium. The Examiner, referring to the abstract from Chemical Abstracts and page 3, lines 1-19 of the document, stated that the substituents on the diallylammonium monomer can be methyl, ethyl, propyl, hydroxyethyl, hydroxylpropyl and

dihydroxypropyl. The Examiner acknowledged that Niike, *et al.* do not expressly teach that the substituent is a dihydroxypropyl group. However, the Examiner alleges that it would have been *prima facie* obvious to have a dihydroxypropyl group as a substituent because it is one of the few known substituents.

The Examiner, referring again to the abstract and column 5, lines 18-28 of the document, stated that the copolymers of Niike, *et al.* are in an emulsion composition. The Examiner further stated that there is water in the emulsion. The Examiner alleged that the water in the emulsion is an inert pharmaceutical adjuvant material.

In the Advisory Action mailed July 18, 2003, the Examiner maintained the position that Claims 71 and 73 are obvious. In particular, the Examiner stated that an "emulsion comprising the polymer and water would read on the claimed invention." The Examiner alleged that because Niike, *et al.* do not have any limitation as to the water employed, employment of non-toxic water in the emulsion is obvious.

B. Appellants' Traversal

Although Appellants submit that Claims 71 and 73 are separately patentable due to the differences in the recited polymers (see complete discussion below), the arguments in favor of patentability are equally applicable to both claims and Appellants are not providing separate argumentation for each rejected claim.

Niike, *et al.* do not teach a pharmaceutical composition comprising a polymer. Rather, Niike, *et al.* disclose an emulsification dispersant containing a copolymer that is advantageously used in paper manufacture. The copolymer of the emulsification dispersant contains an acrylic ester or styrene monomer and an amine- or ammonium-containing monomer. Niike, *et al.* teach that the ammonium-containing monomer can be a disubstituted diallylammonium monomer, however, no working examples of a copolymer containing a diallylammonium monomer are disclosed. Thus, it appears that Niike, *et al.* do not teach or otherwise suggest that a polymer characterized by a diallylammonium monomer substituted with one or two 2,3-dihydroxypropyl groups has any properties to distinguish it from other amine- and ammonium-containing monomers. As such, one of ordinary skill in the art would have had no motivation to select a diallylammonium monomer substituted with one or two 2,3-dihydroxypropyl groups, particularly

for use in a pharmaceutical composition. Furthermore, there would have been no reasonable expectation that a polymer characterized by a diallylammonium monomer substituted with one or two 2,3-dihydroxypropyl groups would be successful as a pharmaceutical composition, let alone a successful fat-binding polymer.

Moreover, the Examiner's assertion that water used to make an emulsion in an industrial process such as that disclosed by Niike, *et al.* is suitable as an inert pharmaceutical adjuvant is baseless. It is difficult to envision how water that has been used in an industrial process could be safe for consumption by a subject. Water used in an emulsion for paper manufacture simply is not an inert pharmaceutical adjuvant, as the polymer in the emulsion process is not a pharmaceutical but rather an agent to facilitate emulsion formation advantageous for paper processing.

As the Examiner has stated, Niike, *et al.* do not have any limitation as to the type of water employed. Although the Examiner asserts that using non-toxic water is obvious, this rejection is made with hindsight based on Applicants' discovery that the polymers described and claimed in the subject application can be useful as pharmaceuticals. One of ordinary skill in the art would not have been motivated to use "non-toxic" pharmaceutical grade water in the emulsions disclosed by Niike, *et al.* since the polymers were not known as pharmaceuticals prior to Applicants' discovery. Certainly, one of ordinary skill in the art would not have appreciated a need to provide non-toxic water and subsequently to ensure that the water is not contaminated in the processes in Niike, *et al.*

In summary, Claims 71 and 73 are not obvious over Niike, *et al.* First, one of ordinary skill in the art would not have been motivated to select polymers specifically having a diallylammonium monomer substituted with one or two 2,3-dihydroxypropyl groups. Niike, *et al.* clearly do not teach any particular advantages of such polymers. Second, the assertion that industrial or laboratory grade water renders pharmaceutical grade water obvious is groundless. Pharmaceutical grade water is for use with pharmaceuticals, not with emulsions for industrial paper processing. As such, one of ordinary skill in the art would have had no motivation to select pharmaceutical grade water (i.e., an inert pharmaceutical adjuvant) since Niike, *et al.* do not teach or suggest pharmaceutical polymers. Thus, both the polymers and the inert

pharmaceutical adjuvants in Claims 71 and 73 are clearly distinguishable from the copolymers and industrial water of Niike, *et al.* and the rejection over Niike, *et al.* should be withdrawn.

C. Groups 1 and 2 Do Not Stand or Fall Together

Groups 1 and 2 (Claim 71 and Claim 73, respectively) are separately patentable, because one of ordinary skill in the art would expect the recited polymers to have different fat-binding properties. The repeat unit of Structural Formula (VI) that is recited in Claim 71 is a poly(diallylamine) repeat unit, where the amine nitrogen is substituted with two dihydroxypropyl groups. The repeat unit of Structural Formula (VII) that is recited in Claim 73 is a poly(diallylamine) repeat unit, where the amine nitrogen is substituted with one dihydroxypropyl group and either a hydrogen atom or a alkyl chain containing 1 to 22 carbon atoms.

One of ordinary skill in the would expect that the repeat unit of Structural Formula (VI) would interact primarily with the polar regions of a lipid due to the presence of the charged amine nitrogen and the highly polar hydroxyl groups on each substituent group of the amine nitrogen. In contrast, one of ordinary skill in the art would expect that the repeat unit of Structural Formula (VII) would interact with both the polar and nonpolar regions of a lipid due to one substituent group on the amine nitrogen having hydroxyl groups while the other substituent group was simply hydrogen or an unsubstituted alkyl group. Accordingly, one of ordinary skill in the art would expect that polymers characterized by these repeat units would not have the same function. Thus, pharmaceutical compositions that include polymers characterized by these repeat units should be separately patentable, and Claims 71 and 73 should not stand or fall together.

CONCLUSION

In view of the foregoing arguments, it is requested that the remaining rejection be reversed and that the application be passed to issue. This Brief is being filed in triplicate.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

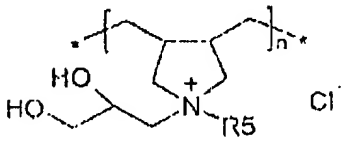
By Jesse G. Feeker

Jesse A. Feeker, Ph.D.
Registration No. 52,883
Telephone: (978) 341-0036
Facsimile: (978) 341-0136

Concord, MA 01742-9133
Date: 2/25/04

APPENDIX

42. A method of treating obesity in a mammal comprising the step of orally administering to the mammal an effective amount of at least one lipase inhibitor and a fat binding polymer, salt, or copolymer thereof, characterized by a repeat unit having the formula:




(VII),

wherein R5 = H, or an alkyl chain from $C_1$ to $C_{22}$.

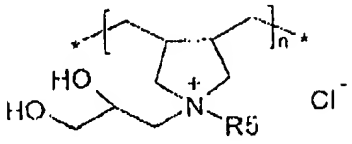
43. The method of claim 42 wherein R5=$CH_3$.

44. The method of claim 42 wherein said polymer is Poly(N,N-diallyl-N-methyl-N-(2,3-dihydroxypropyl) ammonium chloride).

45. The method of claim 44 wherein said lipase inhibitor is tetrhydrolipstatin.

46. A method for treating steatorrhea in a mammal comprising the step of orally administering to the mammal a therapeutic amount of a polymer characterized by having a repeat unit having the formula:

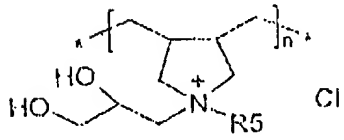
(VII)



Wherein R5 = H, or an alkyl chain from $C_1$ to $C_{22}$

47. A method for treating hypertriglyceridemia in a mammal comprising the step of administering to the mammal a therapeutically effective amount of at least one lipase inhibitor and a polymer characterized by a combination of repeat units having the formula

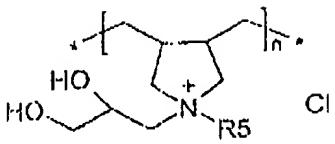
(VII)



Wherein R5 = H, or an alkyl chain from $C_1$ to $C_{22}$, in combination with at least one lipase inhibitor.

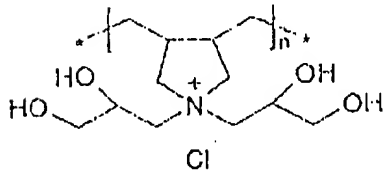
48. A method for reducing the absorption of dietary fat in a mammal comprising the step of orally administering to the mammal a therapeutically effective amount of at least one lipase inhibitor in combination with a polymer characterized by a combination of repeat units having the formula

(VII)




Wherein R5 = H, or an alkyl chain from $C_1$ to $C_{22}$.

56. A method of treating obesity in a mammal comprising the step of orally administering to a mammal an effective amount of a polymer, salt, or copolymer thereof, characterized by a repeat unit having the formula:(VI)

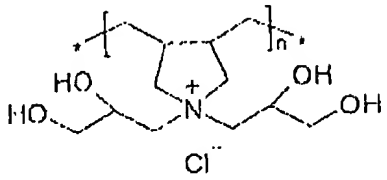



in combination with at least one lipase inhibitor.

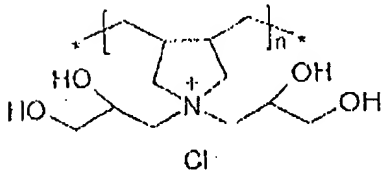
57. The method of claim 56 wherein said lipase inhibitor is tetrahydrolipstatin.

58. A method for treating steatorrhea in a mammal comprising the step of orally administering to the mammal a therapeutic amount of a polymer characterized by having a repeat unit having the formula:

(VI)

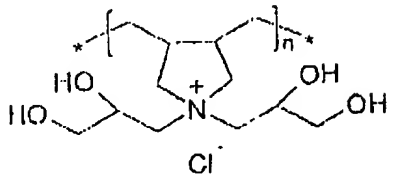



59. A method for treating hypertriglyceridemia in a mammal comprising the step of administering to the mammal a therapeutically effective amount of at least one lipase inhibitor and a polymer characterized by a combination of repeat units having the formula:




(VI).

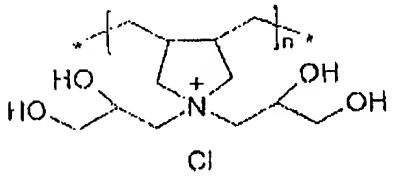
60. A method for reducing the absorption of dietary fat in a mammal comprising the step of orally administering to the mammal a therapeutically effective amount of at least one lipase inhibitor and a polymer characterized by a combination of repeat units having the formula:



(VI).

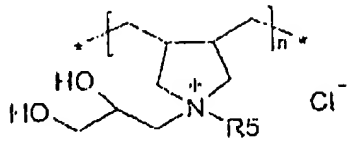
61. The method of claim 56 wherein said polymer is as **Poly**(N,N-diallyl-N,N-di(2,3-dihydroxypropyl)ammonium chloride).

71. A pharmaceutical composition comprising an inert pharmaceutical adjuvant material and a polymer, salt or copolymer thereof characterized by a repeat unit having the formula:



(VI).

73. A pharmaceutical composition comprising an inert pharmaceutical adjuvant material and a polymer, salt or copolymer thereof characterized by a repeat unit having the formula:



(VII),

wherein R5 = H, or is an alkyl chain from $C_1$ to $C_{22}$.